REMARKS

Amendments to the Claims

Claims 4, 7-10, 16 and 19 have been canceled.

Claims 3, 14-15 and 17 have been amended.

New Claims 20-35 have been added.

Claims 3, 14, 15 and 17 as amended, and new Claims 20-23, 25-27 and 33 recite "antigen binding fragment." Support is found in the specification, for example, at page 17, lines 2-8. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 1, lines 5-12 and page 11, lines 10-20.

Claim 3, as amended, and new Claims 20 and 33 recite "ATCC Accession No. PTA-7045" Support for these amendments is found in the specification, as amended, for example, at page 25, lines 16-23. In addition, support for reference to the cell line for the A2 antibody is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Claim 3, as amended, and new Claim 20 recites "inflammatory and immune disease." New Claim 33 recites "inflammatory and immune processes." New Claim 34 recites "wherein said TNFα-mediated inflammatory and immune processes are chronic inflammatory and immune processes." New Claim 35 recites "wherein said TNFα-mediated inflammatory and immune processes are acute inflammatory and immune process." Support for these claim amendments is found in the specification, for example at page 58, line 1 to page 59, line 14. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4. This priority application is incorporated in the subject application by reference on page 1, lines 4-21.

Claim 3, as amended, and new Claims 20 and 33 recites that the antibody or antigen-binding fragment "binds to a neutralizing epitope of human TNFα *in vivo* with an affinity of at least 1 x 10^8 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis." Support is found in the specification, for example, at page 21, lines 16-23; page 60, line 25 to page 61, line 5; and Example X, particularly at page 80, line 24 to page 81, line 12. In addition, support is found in the specification of priority application US Serial No. 07/670,827,

filed March 18, 1991, for example, at page 13, lines 5-8; page 18, lines 17-19; page 20, lines 3-6; and Example X, particularly, at page 67, line 12 to page 68, line 25.

Claim 3 has been further amended and new Claim 33 recites "human constant region." New Claim 20 has recites "human IgG1 constant region." Support is found in the specification, for example, at page 10, lines 8-15; page 17, lines 19-21; page 31, line 6 to page 32, line 2; and page 34, lines 16-21. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 9, lines 21-23; page 12, lines 18-26; page 26, lines 6-19; and page 52, lines 18-20.

Claim 3, as amended, and new Claims 20 and 33 recite that the antibody or antigen-binding fragment competitively inhibits binding of A2. Support is found in the specification, for example, at page 19, line 17 to page 20, line 2 and page 30, lines 5-12. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, line 24 to page 13, line 4; page 14, lines 3-9; and page 19, lines 3-10.

New Claim 21 is directed to the method of Claim 3, wherein said antibody or antigen-binding fragment is of immunoglobulin class IgG1, IgG2, IgG3, IgG4 or IgM. Support is found in the specification, for example, at page 17, lines 19-21; page 31, lines 6-13; and page 125, lines 14-17. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 26, lines 6-19.

New Claim 22 recites "The method of Claim 3, wherein said antigen-binding fragment is selected from the group consisting of Fab, Fab', $F(ab')_2$ and Fv." Support is found in the specification, for example, at page 26, line 4. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 20, lines 16-19.

New Claim 23 recites "The method of Claim 3, wherein the antibody or antigen-binding fragment thereof comprises at least one human framework region." Support is found in the specification, for example, at page 9, lines 8-11; page 31, line 3 to page 32, line 2. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

New Claim 25 is directed to the method of Claim 3, wherein the antibody or antigen-

binding fragment comprises a human constant region and a human variable region. New Claim 26 is directed to the method of Claim 3, wherein the antibody or antigen-binding fragment comprises at least one human light chain and at least one human heavy chain. Support is found in the specification, for example, at page 17, line 24 to page 18, line 16; page 19, lines 1-6; page 31, line 3 to page 32, line 2. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

New Claim 27 recites "The method of Claim 3, wherein said analysis comprises labeling the anti-TNFα antibody or antigen-binding fragment thereof and measuring direct binding of ^{125}I labelled anti-TNFα antibody or antigen-binding fragment thereof to immobilized rhTNFα, and wherein said antibodies are labelled to a specific activity of about 9.7 μCi/μg by the iodogen method." Support for this claim is found in the specification, for example, at Example X, particularly page 80, line 24 to page 81, line 7. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at Example X, particularly page 67, line 12 to page 68, line 18.

New Claim 28 recites "The method of Claim 17, wherein the single or divided dose is about a 5 - 20 mg/kg dose." Support is found in the specification, for example, at page 81, line 21 to page 82, line 8. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 41, line 3-13.

New Claim 29 recites "The method of Claim 3, further comprising administering to the human an amount of an anti-inflammatory agent effective to treat the TNFα-mediated inflammatory and immune disease." New Claim 30 recites "The method of Claim 29, wherein the anti-inflammatory agent is selected from the group consisting of: pentasa, mesalazine, asacol, codeine phosphate, benorylate, fenbufen, naprosyn, diclofenac, etodolac, indomethacin, aspirin and ibuprofen." New Claim 31 recites "The method of Claim 3, further comprising administering to the human an effective amount of an anti-pain agent to treat pain associated with TNFα-mediated inflammatory and immune disease." New Claim 32 recites "The method of Claim 3, further comprising administering to the human an amount of methotrexate effective to treat TNFα-mediated inflammatory and immune disease." Support for this amendment is found in the specification, for example, at page 131, lines 22-28; Example XXI and Example XXII, particularly Table 12 at page 115. In addition, support is found in the specification of

priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 10, line 22 to page 11, line 9 and page 43, lines 1-26.

New Claim 24 is directed to the method of Claim 3, wherein said TNFα-mediated inflammatory and immune disease results in tissue injury. Support for this amendment is found in the specification, for example, at page 2, lines 21-26. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 3, lines 13-20.

No new matter has been added by the amendments. Therefore, entry of the amendments into the application is respectfully requested.

Status of Claims

On page 2 of the Detailed Action, the Examiner states that Claims 1, 3-5 and 7-13 are pending and being acted upon presently.

Applicants note that this is an error. Claims 3-4, 7-10 and 14-19 are being acted upon presently.

Examiner Interview

Applicants thank the Examiner for taking the time to discuss this case, and for providing helpful comments, during the Examiner interview at the United States Patent and Trademark Office held on October 19, 2005.

Amendments to the Specification

Applicants have amended the specification to update the status of related applications.

In regard to the spelling of "Geysen", Applicants have amended the specification to correct the obvious error in the spelling of "Geysen." Applicants submit evidence that the correct spelling is "Geysen" as indicated in the enclosed Abstract (Geysen, H.M. *et al.*, "A Synthetic Strategy for Epitope Mapping", *Peptides, Proceedings of the Tenth American Peptide Symposium* 519-523 (Garland R. Marshall ed., Escom, Leiden, 1988) (Exhibit A)).

Applicants have amended the specification to recite "ATCC Accession No. PTA-7045," and to recite that c134A was deposited pursuant to the Budapest Treaty requirements with the

American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, on September 22, 2005. Support for these amendments is found in the specification, as amended, for example, at page 25, lines 16-23. In addition, support for reference to the cell line for the A2 antibody is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Therefore, entry of the amendments into the application is respectfully requested.

Priority

The Examiner maintains that the filing date of the instant claims is deemed to be the filing date of the priority application USSN 08/570,674, filed December 11, 1995, on the grounds that the previous priority applications do not support the claimed limitations of the instant application, encompassing methods of treating psoriasis.

Applicants have amended Claim 3 to recite a method of treating a TNFα-mediated "inflammatory and immune disease." As discussed above, support for these claim amendments is found in the specification, for example at page 58, lines 2-14. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4. The remaining pending claims are dependent from Claim 3 and are entitled to the same priority date. As indicated above, the new claims find support in the same priority application. The instant claims are entitled to claim the benefit of priority application USSN 07/670,827 (filed March 18, 1991). Priority application USSN 07/670,827 provides sufficient written description and enablement for treating TNFα-mediated human disease, including inflammatory and immune disease. This priority application has been properly referenced on page 1 of the specification in compliance with 35 U.S.C. § 120.

Rejection of Claims 3, 4 and 14-19 Under 35 U.S.C. § 112, first paragraph

Claims 3, 4 and 14-19 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner states that the cA2 antibody must be known and readily available to the public, or obtainable by a repeatable method set forth in the specification, or else a deposit of the cell line/hybridoma may be made in order to satisfy the enablement requirement.

37 C.F.R. § 1.809 (b)(1) states that "[t]he applicant for patent or patent owner shall reply to the rejection under paragraph (a) of this section by (1) In the case of an applicant for patent, either making an acceptable original...deposit, or assuring the Office in writing that an acceptable deposit will be made...." In addition, 37 C.F.R. § 1.809 (d) states that "[f]or each deposit made pursuant to these regulations, the specification shall contain: (1) The accession number for the deposit; (2) The date of deposit; (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) The name and address of the depository."

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to expedite prosecution, and in accordance with 37 C.F.R. § 1.809 (b)(1), on September 22, 2005, Applicants deposited the cell line for the A2 antibody (designation c134A) with American Type Culture collection (ATCC) under the Budapest Treaty. The ATCC accession number is PTA-7045.

The specification at page 25, lines 16-23 has been amended to recite "As examples of antibodies according to the present invention, murine mAb A2 (ATCC Accession No. PTA-7045) of the present invention is produced by a cell line designated c134A." The specification at page 25, lines 16-23 has been further amended to recite "c134A was deposited pursuant to the Budapest Treaty requirements with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, on September 22, 2005."

Further, Claims 4, 16 and 19 have been cancelled. Applicants reserve their rights to file continuing or divisional applications to pursue these claims. Claims 3, 14-15 and 17 have been amended to delete reference to cA2, and Claim 3 has been further amended to recite "ATCC Accession No. PTA-7045" for the cell line of the A2 antibody. Claims 14, 15, 17 and 18 are dependent upon Claim 3, and, therefore, contain the same limitation.

Support for the amendments and the deposit of the cell line for the A2 antibody is found in the specification, for example, at page 25, lines 16-23. In addition, support is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Filed concurrently herewith is a Statement Under 37 C.F.R. §1.804, §1.806 and §1.808.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection to Claims 3, 4 and 14-19 Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 3, 4 and 14-19 as indefinite in the recitation of "cA2". Specifically, the Examiner states that "the use of 'cA2' antibody as the sole means of identifying the claimed antibody renders the claims indefinite because this designation is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct cell lines."

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, Claims 4, 16 and 19 have been canceled. Claims 3, 14-15 and 17 have been amended to delete reference to cA2, and Claim 3 has been further amended to recite "ATCC Accession No. PTA-7045" for the cell line of the A2 antibody. As discussed above, on September 22, 2005, Applicants deposited the cell line for the A2 antibody with ATCC under the Budapest Treaty. The specification at page 25, lines 16-23 have been amended to recite the ATCC accession number, the date of deposit, a description of the biological material and the name and address of the depository. Claims 14, 15, 17 and 18 are dependent upon Claim 3, and, therefore, contain the same limitation.

Reconsideration and withdrawal of the rejection are respectfully requested.

Nonobviousness of Claims 3, 4, 7-10 and 14-19 Under 35 U.S.C. § 103(a)

The rejection of Claims 3, 4, 7-10 and 14-19 as being unpatentable over Adair *et al.* (U.S. Patent No.: 5,994,510) in view of Le *et al.* (WO 92/16553) is maintained for reasons of record.

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to further prosecution, as discussed above, Claims 4, 7-10, 16 and 19 have been canceled. Claim 3 has been amended to recite TNFα-mediated "inflammatory and immune disease", and Claims 14, 15, 17 and 18 depend on Claim 3, thereby rendering the rejection moot. As discussed above, support for these claim amendments is found in the specification, for example at page 58, lines 2-14. In addition, support is found in priority application 07/670,827, filed March 18, 1991, at page 10, line 22 to page 11, line 4. Thus, the claims, particularly as amended, are entitled to priority to 07/670,827 (filed March 18, 1991).

For the reasons of record and for the reasons described herein with regard to priority, Applicants maintain that Le *et al.* (WO 92/16553) and Adair *et al.* are not prior art because the priority date of the subject application (March 18, 1991) precedes the date that Le *et al.* and Adair *et al.* would be effective as prior art. Therefore, neither Le *et al.* (filed March 18, 1992 and published October 1, 1992) nor Adair *et al.* (filed June 1, 1995, issued November 30, 1999) are prior art. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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